AMENDMENT

Please amend the application without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents.

In the Claims

1. (Original) A polynucleotide comprising at least two repeats of a hypoxia response element (HRE), wherein the hypoxia-inducible factor (HIF) consensus binding sites within each of the two repeats are separated by a spacer of at least 20 contiguous nucleotides.

2. (Currently amended) [[A]] The polynucleotide according to claim 1, wherein the HRE repeats are operably linked to a viral promoter.

3. (Currently amended) [[A]] The polynucleotide according to claim 1, wherein said spacer comprises a nucleotide sequence selected from the group consisting of ~~as shown in~~ SEQ. I.D. No. 10 and ~~or~~ SEQ. I.D. No. 11.

4. (Currently amended) [[A]] The polynucleotide according to claim 2 wherein said promoter is selected from an SV40 promoter or an MLV promoter.

5. (Currently amended) [[A]] The polynucleotide according to claim 2, comprising at least four HRE repeats linked to the promoter, wherein at least two of the HRE repeats are positioned upstream (5') of the promoter and upstream the promoter and at least two repeats of the HRE are positioned downstream (3') of the promoter.

6. (Previously amended) The polynucleotide of claim 7, wherein at least three of the HRE repeats are a phosphoglycerate kinase (PGK) hypoxia response element (HRE) repeats operably linked to an SV40 promoter or an MLV promoter.

7. (Currently amended) [[A]] The polynucleotide according to claim 5, comprising at least six HRE repeats, wherein at least three repeats are upstream (5') of the promoter and at least three repeats are positioned downstream (3') of the promoter.

8. (Currently amended) [[A]] The polynucleotide according to claim 1, wherein the HRE repeats are direct repeats.

9. (Currently amended) [[A]] The polynucleotide according to claim 1, wherein the HRE comprises the nucleotide sequence of SEQ ID NO:1 or 2.

10. (Currently amended) [[A]] The polynucleotide according to claim 1, comprising the nucleotide sequence of SEQ ID NO:9.

11. (Currently amended) [[A]] The polynucleotide according to claim 6, comprising

the nucleotide sequence of SEQ ID NO:3, 4, or 5.

12. (Currently amended) [[A]] The polynucleotide according to claim 2, operably linked to a nucleic acid of interest (NOI) such that the polynucleotide directs expression of the NOI in a host cell.

13. (Currently amended) [[A]] The polynucleotide according to claim 12, wherein the NOI encodes HIF-1.

14. (Currently amended) [[A]] The polynucleotide according to claim 13, wherein the promoter lacks a CAAT box sequence.

15. (Currently amended) [[A]] The polynucleotide according to claim 12, wherein the host cell is a tumour cell.

16. (Cancelled)

17. (Currently amended) [[A]] The polynucleotide according to claim 12, wherein the NOI encodes a polypeptide which is cytotoxic.

18. (Currently amended) [[A]] The polynucleotide according to claim 12, wherein the NOI encodes a polypeptide capable of converting a prodrug into a cytotoxic compound.

19. (Currently amended) [[A]] The polynucleotide according to claim 12, wherein the NOI encodes a transcription factor, a metabolic enzyme, a proliferation-regulating protein, or a heat shock protein.

20. (Currently amended) [[A]] The polynucleotide according to claim 12, adapted to deliver the NOI to a mammalian cell.

21. (Currently amended) A ~~polypeptide according to claim 1, disposed in a~~ nucleic acid vector comprising the polynucleotide of claim 1.

22. (Currently amended) The vector ~~polypeptide~~ of claim 21, wherein the vector is a viral vector.

23. (Currently amended) The vector ~~polypeptide~~ of claim 22, wherein the viral vector further comprises a nucleotide sequence selected from the group consisting of (i) a nucleotide sequence encoding an inhibitory RNA molecule capable of effecting the cleavage, directly or indirectly, of VHL RNA; (ii) one or more inhibitory RNA molecules that bind to and prevent VHL RNA processing, expression, or both; and (iii) a nucleotide sequence encoding a polypeptide capable of inhibiting the binding of VHL to Elongin B, Elongin C, or both.

24. (Currently amended) The vector ~~polypeptide~~ of claim 23, wherein said nucleotide

sequence (iii) encodes a non-functional derivative of wild type VHL.

25. (Currently amended) The vector ~~polypeptide~~ of claim 22, wherein the viral vector is a retroviral vector.

26. (Currently amended) The vector ~~polypeptide~~ of claim 22, wherein the viral vector is an adenoviral vector.

27. (Currently amended) The vector ~~polypeptide~~ of claim [[25]] 22, wherein the viral vector is a lentiviral vector.

28-30. (Cancelled)

31. (Currently amended) A method of producing a viral strain which method comprises introducing [[a]] the polynucleotide of claim 2 into the genome of a virus.